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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/874,493	06/05/2001	Ronny van't Oever	6811.US.O1	6161

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EXAMINER

HESS, DANIEL A

ART UNIT

PAPER NUMBER

2876

DATE MAILED: 08/14/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/874,493

Applicant(s)

OEVER ET AL.

Examiner

Daniel A Hess

Art Unit

2876

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 12-21 is/are rejected.
- 7) ☒ Claim(s) 9-11 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on \_\_\_\_ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Specification***

1. The abstract of the disclosure is objected to because it is very short. There is little indication of what is inventive. On the other hand, the 'Summary of the Invention' section appears twice, the first instance being relatively short. It is suggested that the applicant use the first instance of 'Summary of the Invention' as the abstract, in the place of the present abstract. Correction is required. See MPEP § 608.01(b).

2. The disclosure is objected to because of the following informalities: On page 8, line 28 the word 'sphaered' should be 'sphered.' On line 26, the word 'vey' should be 'very.'

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

Art Unit: 2876

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-4, 12-15 and 19-21 are rejected under 35 U.S.C. 103(a) as being obvious over Tycko (US 5,194,909) in view of Kim et al. (US 5,559,037).

The applied reference Kim has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Tycko shows (column 7, line 66; column 4, lines 65-70) the spherizing of red blood samples using spherizing reagent. The solution is (column 8, lines 8-15) a neutrally buffered

Art Unit: 2876

saline solution (7.4 pH). Individual cells are 'entrained' (column 5, line 4). There is a 'stream' (column 15, line 51) of liquid containing the cells. Light of a particular color is shone on the cells (column 5, line 9; column 9, line 41). Tycko further shows that scattering measurements are taken at two particular angles (figures 4 and 5). These are 'forward scattering' measurements (column 5, lines 10-12). Tycko does show the use of plots to correlate the three variables of volume (V), HC and a scatter signal in figures 4 and 5, although he only shows this in two dimensions. However, in doing so, Tycko illustrates the principle of using gridded lines in a third variable to include 3 variables in 2 dimensions. Tycko also shows that a given measurement of scattering at a certain angle forms a single 'equation' for the variables of volume V and hemoglobin concentration HC (see figures 4 and 5). In figures 4 and 5, Tycko effectively shows two such equations.

Tycko fails to specifically note anticoagulant. Tycko also fails to show polarized side-scatter.

Kim shows (column 10, lines 12-15) use of anticoagulant so blood doesn't stick. Kim (column 8, line 35) shows polarized side scatter as a defining feature of red blood cells.

In view of Kim's teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the old and well-known anticoagulant because sticking of blood cells would create a problem for the 'entraining' and 'streaming' process. It also would have been obvious to use side scatter as taught by Kim because this is part of a 'feature space' for the cell measurement (column 8, lines 34 and 35) and more and redundant data is likely to yield greater consistency. Although Tycko fails to show using a surface to carry 5 variables in three dimensions, this follows from Tycko's use of gridded lines to add an extra

Art Unit: 2876

variable in 2-space. To add two extra variables in 3 space, it would be necessary to add sets of gridded lines in two additional variables; this forms a surface. The motive for using a single plot in this manner as opposed to a series of plots as Tycko shows is that more data can be conveyed at once, which is faster and more efficient.

Re claim 2: Tycko shows (column 5, lines 12-20) that the scatter signal is dependent on the index of refraction/hemoglobin concentration and volume of each cell. This is the theory behind figures 4 and 5 of Tycko and is incorporated into Tycko as modified by Kim as applied to claim 1 above.

Re claim 3: Tycko's wavelength of 632 nm (column 6, line 51) falls within this range.

Re claim 4: In Tycko (column 10, lines 7-11) Mie scattering theory is employed to compute what amount to two-dimensional cross sections of the 3-D surface (see figures 3a-3d). The term  $dC/d\Theta$  can be broken down as follows:

$dC$  --- as discussed re claim 2: above, Tycko notes that hemoglobin is a function of the refractive index at a given wavelength.  $d\Theta$  is the difference between each refracted angle and the beam of light.

Re claim 12: The difference between claim 12 and claim 1 is that a different set of three attributes (i) a forward angle scatter; (ii) a light loss, and (iii) a side angle scatter signal are used.

Tycko fails to show the use of (i) a forward angle scatter; (ii) a light loss, and (iii) a side angle scatter signal are used.

Kim shows (column 8, lines 34-35) five properties, ALL, IAS, FL3, PSS, and DSS. ALL is light extinction (column 3, lines 10-15), IAS is a first forward angle scattering (column 3, lines

Art Unit: 2876

15-20) and PSS is polarized side scatter (column 8, line 35). Kim notes (column 8, 45-50) that these elements comprise a feature space.

In view of Kim's teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the old and well-known three features of (i) a forward angle scatter; (ii) a light loss, and (iii) a side angle scatter signal as taught by Kim in the teachings of Tycko as modified by Kim because these represent a permutation of scattering data within the feature space discussed by Kim that incorporates new data which helps to yield greater consistency through reinforcement.

Re claim 13: Claims 1 rejected under 35 U.S.C. 103(a) as being obvious over Tycko (US 5,194,909) in view of Kim et al. (US 5,559,037).

Tycko shows (column 7, line 66; column 4, lines 65-70) the sphering of red blood samples using sphering reagent. The solution is (column 8, lines 8-15) a neutrally buffered saline solution (7.4 pH). Individual cells are 'entrained' (column 5, line 4). There is a 'stream' (column 15, line 51) of liquid containing the cells. Light of a particular color is shone on the cells (column 5, line 9; column 9, line 41). Tycko further shows that scattering measurements are taken at two particular angles (figures 4 and 5). Although he doesn't show explicitly how the angular differentiation is achieved, it is clear he must have a way. Intensities for scattering within these angles is obtained (figures 3 and 4). Tycko shows a means for determining volume and hemoglobin concentration on a cell-by-cell basis: Tycko does show the use of plots to correlate the three variables of volume (V), HC and a scatter signal in figures 4 and 5, although he only shows this in two dimensions.

Tycko fails to show separate analysis for white blood cells.

Art Unit: 2876

Kim shows (column 2, lines 40-50) separating out WBC's for independent analysis.

In view of Kim's teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the old and well-known separation of WBC's for independent analysis as taught by Kim into the teachings of Tycko because white blood cell data lends itself to a set of applications that red blood cell data does not, such as the immune system.

Re claim 14: Tyco shows in figures 4 and 5 scattering for two different forward angles. Tyco also notes a correlation between the scatter data and shape of the cell (column 6, lines 1-10).

Tycko fails to show the use of a side angle scatter signal.

Kim shows (column 8, lines 34-35) five properties, ALL, IAS, FL3, PSS, and DSS. PSS is polarized side scatter (column 8, line 35). Kim notes (column 8, 45-50) that these elements comprise a feature space.

In view of Kim's teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the old and well-known three features of a side angle scatter signal as taught by Kim in the teachings of Tycko as modified by Kim because this represents a portion of scattering data within the feature space discussed by Kim that incorporates new data which helps to yield greater consistency through reinforcement.

Re claim 15: Tycko fails to show the use of (i) a forward angle scatter; (ii) a light loss, and (iii) a side angle scatter signal are used.

Kim shows (column 8, lines 34-35) five properties, ALL, IAS, FL3, PSS, and DSS. ALL is light extinction (column 3, lines 10-15), IAS is a first forward angle scattering (column 3, lines



Art Unit: 2876

15-20) and PSS is polarized side scatter (column 8, line 35). Kim notes (column 8, 45-50) that these elements comprise a feature space.

In view of Kim's teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the old and well-known three features of (i) a forward angle scatter; (ii) a light loss, and (iii) a side angle scatter signal as taught by Kim in the teachings of Tycko as modified by Kim because these represent a permutation of scattering data within the feature space discussed by Kim that incorporates new data which helps to yield greater consistency through reinforcement.

Re claim 19: Tycko's wavelength of 632 nm (column 6, line 51) falls within this range.

Re claim 20: Clearly Tycko had a HeNe laser in mind when he named a 632 nm light source.

Re claim 21: Employing the principle of equivalency, the examiner notes that although it is not clear whether Tycko has as his spherizing agent a non-ionic surfactant, as long as the effect of spherizing red blood cells is achieved, the type of spherizing agent is not critical.

6. Claims 5-8 and 16 are rejected under 35 U.S.C. 103(a) as being obvious over Tyco as modified by Kim (US 5,559,037) as applied to claim 1 above, in further view of Kim (US 5,691,204).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the

Art Unit: 2876

inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Tyco fails to show the explicit separation of reticulocytes using dye.

Kim (US 5,691,204) shows (column 4, line 25 to column 5, line 17) the separation of reticulocytes using dye. The dye is fluorescent (column 4, line 53).

In view of Kim, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the old and well-known staining of reticulocytes because they are a different type of particle and signals from each type of particle should be separated for clarity.

Re claims 6 and 7: Tycko as modified by Kim as applied to claim 5 above fails to show a 2-D cytogram of either light-loss or forward scatter with fluorescence in order to form a gate to exclude white blood cells, nucleated RBC's and platelets.

Art Unit: 2876

Kim (US 5,559,037) shows that to exclude white blood cells/nucleated RBC's, platelets (column 3, lines 8-15) a cytogram can be constructed. It is possible to identify 'abnormal blood' including NRBC's, WBC's, and platelets by the use of cytograms (column 10, line 60 to column 11, line 10). Kim shows the claimed cytograms, as can be see in figs 12b (light loss-fluorescence) and figure 12a (forward scatter vs. fluorescence) (see column 3, lines 15-20 for a key of these figures).

In view of Kim's teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the old and well-known 2-D cytogram of either light-loss or forward scatter with fluorescence in order to form a gate to exclude white blood cells, nucleated RBC's and platelets as taught by Kim into the teachings of Tycko as modified by Kim because this helps eliminate noise when evaluating normal RBC's.

Re claim 8: If the reticulocytes have been separated out as per claim 5 above with fluorescent dye, the capability has been created to analyze those cells separately, using the same process as for RBC's. The motive to do so is that reticulocyte properties may contain diagnostic value in their own right.

7. Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tycko as modified by Kim as applied to claim 13 above, and further in view of Kirchanski et al. (US 4,882,284).

Tycko as modified by Kim, as discussed above, could include measurement of any of ALL, IAS, FL3, PSS, and DSS.

Art Unit: 2876

Tycko as modified by Kim fails to show determination of internal cell complexity and granularity.

Kirchanski shows (column 6, lines 40-50) that internal cell structure and granularity can be determined for white cells using scattering data.

In view of Kirchanski's teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the old and well-known use of scattering data to determine internal cell complexity and granularity as taught by Kirchanski in the teachings of Tycko as modified by Kirchanski because these determinations can aid in the diagnosis of blood ailments.

***Allowable Subject Matter***

Claims 9-11 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is an Examiner's statements of reasons for the indication of allowable subject matter:

Re claims 9 and 10: The best prior art of record, Kim (US 5,559,037), uses a two-dimensional cytogram to differentiate particles that are not red blood cells. Kim does not, however, use any distance from a cell point on a plot to an expected point in order to measure the occurrence of oddly-shaped red-blood cells. Also, this use of distance for determining abnormally shaped RBC's is not shown in the prior art of record.

Art Unit: 2876

Re claim 11: The examiner did not find within the most relevant art of record, including Tycko and Kim, any indication of the use of symmetry about a pre-established plot, either in two or three dimensions, as a measure of system standardization. Although this can be regarded as a good indication that the system is 'in tune' the examiner did not find indication of this in the relevant art.

### *Conclusion*

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Altendorf (US 6,067,157), Rodriguez et al. (US 5,616,501), Frank et al. (US 5,798,827), Colella (EPO 0 545 314 A1), and Tsuji (US 4,586,190) all show hemoglobin measurements using various optical techniques.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel A Hess whose telephone number is (703) 305-3841. The examiner can normally be reached on 8:00 AM - 5:00 PM M-F.

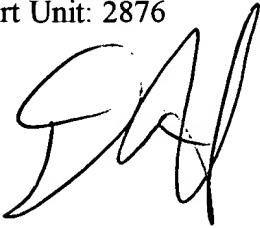
10. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Lee can be reached on (703) 305-3503. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7722 for regular communications and (703) 308-7722 for After Final communications.

11. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0956.

Application/Control Number: 09/874,493

Page 13

Art Unit: 2876

A handwritten signature in black ink, appearing to be 'DAH' with a large, stylized 'H'.

dh

August 2, 2002

Daniel A Hess  
Examiner  
Art Unit 2876

A handwritten signature in black ink, appearing to be 'KDF' with a large, stylized 'F'.

KARL D. FRECH  
PRIMARY EXAMINER